Remarks

Claims 1-34 are pending in the application. Claims 1, 14-17, 32, and 33 have been amended. Claims 8-13, 21-31 and 34 are withdrawn from consideration as directed to a non-elected invention.

Claim amendments

Claims 14 was rewritten as an independent claim, and claims 15-17 and 33 were amended to depend from claim 14. Support for the amendments to claims 14-17, 32, and 33 can be found at least in claims 1 and 13 as originally filed. Claims 1, 14, and 32 were amended to reflect that one or more of R₂ and R₃ may include an alkoxy moiety. Support for the amendments can be found at least at paragraphs 16 and 17. Claim 1 was amended to replace "M+" in the chemical structure of R₁ with "M", consistent with the subsequent occurrence of "M" in claim 1. Support for the amendment can be found in claim 1 as originally filed and at paragraphs 21 and 22 of the specification.

Clarification of claim status

In a November 28, 2005 telephone conference between Examiner Anthony and the undersigned, the Examiner acknowledged that claim 32 is properly included in elected Group I and should have been examined with the other Group I claims. The Examiner indicated that the §102(b) and §103(a) rejections over Bruening et al. are applied to claim 32.

Election / Restriction Requirement

The Examiner has set forth a restriction and an election of species requirement. Group I, claims 1-20 and 32-33, is drawn to a composition comprising a modified solid support that is bonded to a silicon atom and a method of making the solid support. Group II, claims 21-31 and 34, is drawn to a composition comprising a solid support that is bonded to a carbon atom and a method of making the modified solid support. The Examiner also asserts that the application contains claims to two patentably distinct species of the claimed invention: species wherein the R1 moieties contain a metal ion salt and species wherein the R1 moieties are in the form of free acids.

Applicants affirm election of Group I claims and species having an R1 moiety containing a metal ion salt, with traverse.

The Manual of Patent Examining Procedure ("MPEP") states that:

If the search and the examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions.

MPEP § 803. Applicants respectfully submit that the compounds of the present invention could be examined together without placing any serious burden on the United States Patent and Trademark Office. In the interest of administrative efficiency, Applicants respectfully request that the restriction requirement be withdrawn.

Claim Objections

Claim 14 was objected to as being dependent on non-elected base claim 13. Claim 14 was amended to independent form. Applicants request that the objection be withdrawn.

Rejections Under Section 102(b)

Claims 1-7, 14, 18-20 and 32-33 were rejected under 35 U.S.C. §102(b) as anticipated by Bruening et al. (U.S. Patent No. 5,250,188). The Examiner characterizes Bruening et al. as teaching a method for the quantitative removal and concentration of desired molecules or ions, such as gases, anions and amino acids, from a source solution, which comprises bringing the source solution into contact with a solid cation-ligand-matrix consisting of a cation complexed to a ligand molecule covalently bonded to a matrix consisting of an organic spacer bonded to a solid inorganic support through a silicon atom. (Office Action at page 5). Citing to column 5, lines 24-43 of Bruening et al., the Examiner asserts that one of the preferred ligands of the Bruening et al. solid cation-ligand-matrix are amino acids. The Examiner concluded that Applicants' choice of "nitrilotriacetic acid (NTA) as the ligand would have been at one (sic) envisaged since NTA are very well known amino acids." (Office Action at page 6).

Applicants respectfully submit that none of claims 1-7, 14, 18-20, 32, and 33 is anticipated by Bruening et al. because the reference fails to teach each and every element of the claims. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). "The elements must be arranged as required by the claim, but this is not an

ipsissimis verbis test, i.e., identity of terminology is not required." *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). *MPEP § 2131*.

The composition of claim 1 has the following structure:

solid support
$$-\begin{bmatrix} R_2 \\ S_1 \\ R_3 \end{bmatrix}$$
 n

wherein R₁ is

$$X \longrightarrow NR_4 \longrightarrow C \longrightarrow CH_2 \longrightarrow N(CH_2COO^-)_2M$$

X is a substituted or unsubstituted alkylene moiety, a substituted or unsubstituted aralkylene moiety, or a substituted or unsubstituted arylene moiety; and R₄ is a hydrocarbon moiety, a substituted hydrocarbon moiety, or a hydrogen atom. The other substituents are defined as set forth in claim 1. Claims 2-7, which depend directly or indirectly from claim 1, are drawn to compositions having at least the features set forth above. Independent claim 14 and its dependent claims 15-20 are drawn to methods of making a composition having the features of claim 1. Claim 33 is drawn to a composition made by the process of claim 14. Independent claim 32 is drawn to a species of the composition of claim 1 having the following structure:

Bruening et al. discloses a solid cation-ligand-matrix of the general formula Matrix-L-M, wherein M is a metal cation, L is a coordination ligand "consisting of" an organic molecule known to chelate metal cations, and Matrix is a member having the formula:

wherein B is a spacer grouping having from 1 to 10 carbon atoms.

Apparently, the Examiner considers R₁ of the claimed invention to be equivalent to B-L-M of Bruening et al, with L-M of Bruening et al. corresponding to

and B corresponding to X-NR₄ of Applicants' invention.

Nitrilotriacetic acid was not specifically disclosed as being suitable for use as a ligand. To the contrary, at column 7, line 42, NTA was listed as a "desired molecule", i.e., a molecule that could be removed or concentrated from an admixture of other molecules in a solution using a solid cation-ligand-matrix (column 1, lines 8-11). Additionally, NTA is disclosed as being potentially useful as a "receiving solution" (column 10, lines 64-68), which is apparently synonomous with an elution buffer.

Bruening et al. does not teach using NTA specifically to form a ligand, nor does Bruening et al. teach <u>how</u> such a ligand would be covalently bonded to B (i.e., what the covalent bond between the spacer and an NTA-based ligand would be). Therefore, Bruening et al. fails to teach each and every element of the claimed composition.

Contrary to the Examiner's characterization of NTA as being "a very well known amino acid", NTA is not an amino acid. Amino acids are understood by those of ordinary skill in the art to encompass a class of molecules that contain both amino (NH₂) and carboxylic acid functional groups. In contrast, NTA lacks an amino group and is, therefore, not an amino acid. To the contrary, NTA is, in fact, a <u>tertiary</u> amine having the following structure:

$$\begin{array}{l} {\rm CH_2COOH} \\ {\rm I} \\ {\rm N-CH_2COOH} \\ {\rm I} \\ {\rm CH_2COOH} \end{array}$$

Bruening et al. provides a listing of generic classes of unspecified potential ligands. Ligands disclosed as being most effective "are generally members selected from the group consisting of amines, pyridines, amino acids, thiols, phenantrolines, hydroxamic acids, oximes, amides, thioethers, and combinations thereof" (column 5, lines 39-43). Applicants acknowledge that as a tertiary amine, NTA falls within the scope of one of nine broad classes of compounds disclosed as being potentially useful as a ligand. However, from among innumerable compounds encompassed by that listing, which could be bonded in various ways to one of several different spacers to generate countless possible compositions, Bruening et al. describes and exemplifies the preparation of only four such compositions (column 8, Examples 1-4).

Applicants direct the Examiner's attention to Bruening et al. column 5, lines 24-28, at which the ligand is defined as one that will complex with the cation without using all of the coordination sites available to that cation in the formation of complexes or which allows for ion pairing interaction of the cation to be maintained. A matrix-ligand-cation having a net positive charge is essential to operability in the methods of Bruening et al. Therefore, Applicants' claimed composition would be inoperative in the method of Bruening et al. when the metal ion is neutralized by the two carboxylic acid residues of the NTA-based moiety (i.e., the metal ion is +2 or lower). Therefore, the composition of claim 32, which has nickel with an oxidation state of +2, is not anticipated by Bruening et al.

As explained above, Bruening et al. does not disclose the claimed compounds. Applicants do not concede that Bruening et al. teaches a genus that encompasses Applicants' claimed composition. However, for the sake of argument, even if Bruening et al. teaches the genus, the claimed species is not anticipated by Bruening et al. The MPEP states that

[w]hen the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated.

MPEP §2131.02 citing Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Interf. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. In re

Petering, 301 F.2d 676, 133 USPQ 275 (CCPA 1962). MPEP §2131.02 (Italics and underlining added for emphasis).

Applicants submit that the disclosure of Bruening et al. is not sufficiently limited or well delineated to anticipate the claimed invention. As noted above, the list of preferred ligands disclosed by Bruening et al. includes "members selected from the group consisting of amines, pyridines, amino acids, thiols, phenantrolines, hydroxamic acids, oximes, amides, thioethers, and combinations thereof", and thus encompasses a vast number of compounds, particularly when combined with a variety of spacer groups and metals to generate innumerable combinations. Given the large number of possible combinations encompassed by the nine classes of compounds listed as potential ligands, one of ordinary skill in the art could not draw the structural formula or write the name of each of the compounds included in the generic formula. Therefore, only those compounds specifically disclosed in Bruening et al. can be "at once envisaged" from its disclosure.

In the Examples provided in Bruening et al., the ligand matrix was prepared by reacting 3-glycidoxypropyltrimethoxysilane with ethylenediamine (Example 1), ethanedithiol (Example 2), triethylene tetraamine (Example 3), or L-tyrosine (Example 4). In each case, the ligand contains either a free amino group or a free thiol or sulfhydryl group that participates in a reaction such that the ligand is bonded to the spacer. The reaction is illustrated below for L-tyrosine.

$$\begin{array}{c} \text{MeO} \\ \text{MeO} \\ \text{Si} \\ \text{MeO} \\ \text{3-glycidoxytrimethoxysilane} \end{array} \\ \begin{array}{c} \text{COOH} \\ \text{H}_2\text{N} \\ \text{L-tyrosine} \end{array}$$

Because NTA does not have a free amino group or thiol group, it would not react in the same way as those compounds exemplified as ligands in Bruening et al. Clearly, based on the Examples of Bruening et al., one of ordinary skill in the art would not at once envisage Applicants' claimed invention.

Thus, Applicants submit that one of ordinary skill in the art would not "at once envisage" the compositions of claim 1 or 32 or any claim dependent therefrom. Similarly, claim 14 is directed to a method of making the compound as claimed in claim 1. Thus, Applicants submit that claim 14 and any claims dependent on claim 14 are patentable over Bruening et al. for at least the reasons expressed above with respect to claim 1. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

Rejections Under Section 103(a)

Claims 1-7, 14, 18-20, 32, and 33 are rejected under 35 U.S.C. § 103(a) as obvious over Bruening et al. Applicants respectfully submit that the Office Action fails to set forth a *prima facie* case of obviousness, which requires: 1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the teachings; 2) a reasonable expectation of success; and 3) the references must teach or suggest all the claimed limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Bruening et al. does not teach or suggest all of the elements of claims 1, 14, 32 or of any claim dependent therefrom, as explained in detail above in response to rejection of claims under 35 U.S.C. §102(b).

Furthermore, Bruening et al. provides no motivation to modify the compositions disclosed therein to make Applicants' claimed compositions. Bruening et al. teaches that NTA is a "desired" molecule, i.e., one that can be isolated using the disclosed compositions, and that NTA can be used as a "receiving solution" (i.e., an elution buffer) in the disclosed methods. One of ordinary skill in the art would not be motivated to modify Bruening et al. to make the claimed compositions, because there is no disclosure that NTA would be a suitable ligand in the disclosed matrix-ligand-cation complexes.

Applicants do not concede that Bruening et al. teaches a genus that encompasses Applicants' claimed composition. However, for the sake of argument, even if Bruening et al.

teaches a genus encompassing the compositions of any of claims 1-7, 14, 18-20, 32, and 33, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. MPEP § 2144.08 *citing In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994). A *prima facie* case of obviousness also requires that one of ordinary skill in the art would have been motivated to select the claimed species from the disclosed prior art genus. See, e.g., *In re Ochiai*, 71 F.3d at 1569-70, 37 USPQ2d at 1131; *In re Deuel*, 51 F.3d at 1557, 34 USPQ2d at 1214 ("[A] prima facie case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art." (emphasis in original)); *In re Jones*, 958 F.2d at 351, 21 USPQ2d at 1943-44 (Fed. Cir. 1992); *In re Dillon*, 919 F.2d at 692, 16 USPQ2d at 1901; *In re Lalu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984) ("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound."). MPEP § 2144.08(II)(4).

Bruening et al. does not provide motivation to select the claimed species from the disclosed genus, which is so vast that it is impossible to number, let alone draw or name, its members. There is no express teaching that would have provided motivation to make the selection, nor is there structural similarity between Applicants' claimed compositions and those exemplary compounds taught by Bruening et al. that would have motivated one of ordinary skill in the art to select Applicants' claimed compositions.

In view of the foregoing, Applicants respectfully submit that the Examiner has not set forth a *prima facie* case of obviousness for any of claims 1-7, 14, 18-20, 32, and 33 and request that the rejections be withdrawn.

Applicants respectfully submit that the claims as amended are in condition for allowance. Should the Examiner feel that anything warrants further discussion, the Examiner is encouraged to contact the undersigned at the phone number below.

Enclosed is check in the amount of \$120.00 in payment of the fee required under 37 CFR § 1.17(a)(1). No other fee is believed due in connection with this submission. In the event that any other fee is owing, please charge or credit Deposit Account No. 50-0842 for such fee.

Respectfully submitted,

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